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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,296	09/15/2005	Ales Franc	J187-028 US	1964

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,296	FRANC ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. The response filed on **11/4/08** has been entered.

2. Applicant's arguments filed on 11/4/08 have been fully considered but they are not deemed to be persuasive.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1-25 are pending in this office action.

5. The rejection of claims 1 and 20-25 under 35 U.S.C. 112, first as failing to comply with the written description rejection requirement is withdrawn due to the amendment of the claims.

6. The rejection of claims **1-25** under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-7 and 13- 19** of U.S. Patent Application No. **11574929** is withdrawn due to the filing of a Terminal Disclaimer.

7. The rejection of claims **1-25** under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-7 and 13- 19** of U.S. Patent Application No. **11574929** is withdrawn due to the filing of a Terminal Disclaimer.

8. The rejection of claims 1 and 20-25 under 35 U.S.C. 112 second paragraph, as being indefinite is withdrawn due to the amendment of the claims.

9. Claims 1-11 and 20-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mckeage et al. (1995) in view of Zak et al., (US 6,503,943) and Collaueri et al., (US 6,221,393) further in view of Keppler et al., (US 5,256,653) and Calanchi et al. (US 5,900,252) as evidence by Swarbrick-Encyclopedia (1998) for the reasons made of record in Paper No. 20080609 and as follow.

Applicant argues that "when assessing whether a technical solution is or not obvious from the prior art two items should be taken into consideration, the technical problem to be solved and the technical solution by which the inventors solve such technical problem". Applicant also argues that Zak has no relevance to the rejection since it does not hint on any feature of claim 1, and that the Mckeage ,Keppler and Calanchi when considered separately without combining them with further prior art have no relevance to the present solution.

Applicant also argues that the present solution would not have been derived from neither Collaueri and Swarbrick, and that Callaueri focused on hydrophilic xanthan

gums having quite different properties than those of the polysaccharide used in the present solution. Additionally and Collaueri does not mention the tetravalent platinum complexes, and wet granulation. Lastly, Applicant argues that the Encyclopedia of Pharmaceutical Technology only provides a general definition of the granulation.

In response, with regards to the argument that in assessing whether a technical solution is obvious, the claims are not directed to solving a technical solution but merely to a pharmaceutical composition containing platinum complex in a mixture of at least one pharmaceutical acceptable excipient formed of a granulate with particles smaller than 0.5 mm in size. Accordingly, the combination of references are *prima facie* obvious for one of ordinary skill in the art to have used the teachings of the prior art to obtain the claim invention with a reasonable expectation of success.

Applicant is further incorrect that Zak does not contribute to the instant claim 1. Zak was introduced to show that inclusion of excipients to form a platinum complex were known in the prior art before filing of the instant invention, and ties in the teachings of Mckeage. Zak also is employed for its teaching that the platinum complex is (OC-6-43) Bis(acetato)-(1-adamantylamine)-amine-dichloroplatinum (see col. 3, lines 48-51, as required by instant claim 4). Thus compounds of claims 1and 4 are obvious variations of instant formula I.

With regards to Mckeage et al., Keppler and Calanchi, as correctly stated by Applicant, the combination of the references would render the claims obvious. Applicant should note that the rejection was made under 103 and not 102, so

obviousness is established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so is found in either the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the combined teachings of the references would have suggested to those of ordinary skill in the art to formulate a pharmaceutical composition containing a platinum complex, for the reasons made of record.

As to the argument that Collaueri does not teach a platinum complex, this is irrelevant in this 103 rejection, because Collaueri is used to show that granules entering into pharmaceuticals compositions are advantageously prepared from a polysaccharide having particles less than 100 µM, which is less than 0.5 mM, and therefore is alternatively relevant to the formulation, itself.

The statement that different polysaccharides are used in Collaueri is also found not persuasive because the skilled artisan would have been motivated to employ polysaccharides other than xanthum gums in a wet granulation process with a neutral saccharide and a polysaccharide, as claimed in instant claim 2, because no specific type of polysaccharide is recited in instant claims 2 and 6 (for example). Applicant should also note that Collaueri teaches the composition is produced or processed by wet granulation, as stated in the last office action of record.

In summary, Mckeage et al teach a composition comprising a platinum complex, wherein the complex is JM216 (known as [bis-acetato-amine-dichloro-cyclo-

hexaylamine-platinum(IV)), and wherein the composition comprises excipients such as microcrystalline cellulose, starch, lactose and magnesium stearate as the slipping agent (using the specification as a dictionary) in the form of capsule, (see page 451 and 452, as required by instant claims 1, 3 and 5-7).

However Mckeage fails to teach the instantly claimed compound of claim 4. Mckeage also fails to teach the composition in an excipient formed by granulate with particles smaller than 0.5 mm with at least one neutral saccharide and at least one modified polysaccharide.

Zak et al teach a pharmaceutical composition, as a therapy for oncological disease, containing platinum complex and at least a pharmaceutical excipient. See col. 3, lines 9-15.

With regard to claims 1 and 4, the platinum complex is (OC-6-43) Bis(acetato)-(1-adamantylamine)-amine-dichloroplatinum, see col. 3, lines 48-51. Zak teaches A is NH3 and A' is an amine group containing 1-18 carbons, B is a carboxylate group, thus the compound 4 and X is halogen, See col. 2, lines 1-30 as required by instant claims 1, 4 and 20-25.

However, Zak fails to teach the composition in an excipient formed by granulates with particles smaller than 0.5 mm with at least one neutral saccharide and at least one modified polysaccharide.

Collaueri et al. teach granules entering into pharmaceuticals compositions are advantageously prepared from a polysaccharide having particles less than 100 μM, which is less than 0.5 mM, wherein the polysaccharide is mixed with lactose. See col.

2, lines 56-61 and col. 5, lines 37-42. Table 1 teaches the procedure is by wetting. See col.'s 7 and 8. It is also noted that the particle size is based on the release of the active agent over the desired period of time. See col. 3, lines 34-65.

However Collaueri et al. fails to teach the composition comprising a platinum complex.

Keppler et al. teach platinum complexes compositions (with regards to instant claims 2 and 11) wherein the concentration of the excipients is based on the concentration of the active agent , which is within the purview of one of ordinary skill in the art to modify. Also the Keppler teaches tablets can be made with coating materials and delayed dissolution and absorption of the pharmaceutical in the gastrointestinal tract improves tolerability, protraction or delayed action. See col. 7, lines 45-50 and col. 8, lines 57-67. Please note that lactose (a neutral saccharide, maize starch and gum) is taught as an excipient. It is well known in the art that tablets are coated and the type of release pattern will depend upon the tablet coating, which is then subject to enterosolvent dissolution in the bowel as taught by Keppler et al. (see col. 8, lines 57-67 as required by instant claims 8-9).

However, Keppler fails to teach wet granulation.

Calanchi et al. teach a targeted coated drug release formulation having 0.1 mm size for delivery of drugs to the intestinal comprising methacrylic acid, cellulose acetate, see col. 2, lines 38-60 and col. 3, lines 5-42 as required by instant claims 10-11. Calanchi teaches coating tablets with membranes that are pH dependent and which

remain intact in the stomach dissolves when it reaches the desirable pH. See col. 1, lines 57-67.

However Calanchi fails to teach the composition comprises platinum complexes.

It would have been obvious to one of ordinary skill in the art to formulate a pharmaceutical composition to comprise excipients such as lactose and starch because similar formulation have been used in the prior art by Mckeage et al. (see page 452). One of ordinary skill in the art would expect the compounds of instant claims 1, 4 and 20 to function the same as that of Mckeage et al. because the only difference is the substitution of the adamantly amine at A' which is within the species selection of instant claim 1. Also one of ordinary skill in the art would have been motivated to substitute the Mckeage compound with that of Zak because Zak et al teach the instantly claimed compound and it would have been expected that Zak's compound would be capable of forming a granulate with acceptable pharmaceutical excipients having size smaller than 0.5 mm when a polysaccharide and an excipient is used, as taught by Collaueri et al. Complexes of platinum have been used with excipients such as lactose and starch in the prior art prior to the claimed invention. Taking into account, the teaching of Collaueri et al that granules entering into pharmaceuticals compositions are advantageously prepared from a polysaccharide having particles less than 100 μM, which is less than 0.5 mM, it would have been obvious to one of ordinary skill in the art to combine the teachings of those listed above and formulate a pharmaceutical with the claimed characteristics based on the form of release of the active agent. The excipients as taught by Encyc. Pharm. Tech teaches wet granulation having size of 0.5-1.5 mm for

the process of producing tablets to improve the flow property as already discussed above (i.e., as it relates to release rate). Therefore, one of ordinary skill in the art would have been motivated to have the excipients in a particle size of 0.5 mm or less because particle size relates to the rate of release of the active agent.

One of ordinary skill in the art would have been motivated to further add other excipients as a coating agent because, based on the type of diseases taught by Calanchi et al., it is important that drugs are transported intact into the place in which they will carry out their pharmacological action. Therefore it is necessary to delay release of the drug. See also col. 2, lines 1-5. The combined art are well within the purview of one of ordinary skill in the art to make a pharmaceutical composition of instant claim 4 for example, that is of a delayed release character having small size because it is well known that the smaller the units, the wider the distribution in the gastrointestinal tract. See col. 2, lines 38-47 of Calanchi et al.

With regards to the specific concentrations of the excipients (as required by instant claims 2 and 9-11), the determination of a dosage having the optimum therapeutic index is well within the level of the ordinary skill in the art, and the artisan would be motivated to determine the optimum amounts to get the maximum effect of the drug, hence the reference makes obvious the instant invention.

The courts have held in *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) that where the prior art discloses subject matter where there is reason to believe that inherent functions are cited for an identical product to that instantly claimed, the burden is shifted to the applicants to "prove that the subject matter shown to be in

the prior art does not possess characteristics relied on" (205 USPQ 594, second first full para.).

12. Claims 12-19 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mckeage et al. (1995) in view of Zak et al. (US 6,503,943) and Collaueri et al., (US 6,221,393), further in view of Keppler et al., (US 5,256,653) and Calanchi et al. (US 5,900,252), as evidence by Swarbrick-Encyclopedia of Pharmaceutical Technology (1998), as applied to **claims 1-11 and 20-25** for the reasons made of record and as follows.

The above argument and response also applies here in its entirety.

Keppler et al. teach pharmaceuticals are prepared by wet mixing the active substance with the pharmaceutical vehicles, which can then be dispersed into capsules, wherein the coating is an inert closing layer that enables the control release of the active substance, as required by instant claims 12-19. See col. 7, lines 41-49, col. 8, lines 57-67, col. 9, lines 4-15. Lastly, it is obvious that the formation of a tablet is "performed in equipment", as recited in claims 14 & 16.

For the same reason given above, one of ordinary skill in the art would have been motivated to manufacture a pharmaceutical composition containing platinum complexes having the characteristics of granules smaller than 0.5 mm prepared by wet granulation that is capable of having a control release formulation.

10. No claim is allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MICHAEL HARTLEY can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. V. G./
Examiner, Art Unit 1618
1/9/09

/Robert C. Hayes/
Primary Examiner, Art Unit 1649